February 10, 1951.

Dr. L. L. Cavalli,
Serotherapeutic Institute,
Via Darwin 20,
Milan, Italy.

Dear Cavalli:

Thank you very much for your permission to reprint the note on chloromycetin resistance, and for communicating with the editors.

I am sorry to hear that you had made an unsuccessful attempt to find a followship to visit the States; it sounds as if the main bar was the short term that you indicated for your visit; six months is usually the minimum time for which the foundations will underwrite a followship, and they usually prefer a full year.

There is one particular point in connection with your chloromycetin work which I wonder if you can enlighten me about. It should be possible to have a transgressive segregation in crosses between separately developed partially resistant mutants, that is if, by chance, the two incompletely resistant cultures had accumulated different or complementary resistance mutations. Has this been found? It might represent an even stronger argument for the genic basis of quantitative resistance. To follow this possibility further, it might be possible to select for fully resistant recombinations from partially resistant parents with a single selective agent, namely the higher chloromycetin concentration. Finally, do you think that there might be some chance of finding a rather high proportion of demonstrable recombinants in the culture resulting from the slow "entrainment" of a mixture of parents in completel It occurs to me that this might be the basis of a more realistic model system to answer the question whether recombination at the rather low frequencies so far found can be of adaptive value to bacteria.

Atwood, at Columbia, has been doing some very interesting work lately on the cyclic development of bacterial populations in serial subculture. Using an h/ mutation proportion in h- cultures as a marker, he finds that bacterial cultures are repeatedly replaced by new elements which are very slightly better adapted to the medium in which the cultures are grown. This results in an apparent stabilization of mutant frequencies at levels far below the calculated mutational equilibrium. Recombination might play some role in these phenomena too. The general point is that polygenic systems are precisely those in which recombination might be expected to play some natural part.

Most of my efforts now are devoted to summarizing the experimental results with diploid segregations, and in strain cross tests to find optimal material.

sincerely,